FORM PTO-1390 (REV 12-29-99)

U S DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

ATTORNEY'S DOCKET NUMBER: SOM01 P329A

U S. APPLICATION NO (If known, see 37 CFR 1 5): 09/807676

INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/US99/22940	13 October 1999 (13.10.99)	13 October 1998 (13.10.98)

TITLE OF INVENTION: MULTI-CHANNEL NON-INVASIVE TISSUE OXIMETER

APPLICANT(S) FOR DO/EO/US: BARRETT, Bruce J., et al.

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. [X] This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. [ ] This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. [ ] This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).
4. [X] A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.
5. [X] A copy of the International Application as filed (35 U.S.C. 371(c)(2))
   a. [ ] is transmitted herewith (required only if not transmitted by the International Bureau).
   b. [ ] has been transmitted by the International Bureau.
   c. [X] is not required, as the application was filed in the United States Receiving Office (RO/US).
6. [ ] A translation of the International Application into English (35 U.S.C. 371(c)(2)).
7. [X] Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
   a. [ ] are transmitted herewith (required only if not transmitted by the International Bureau).
   b. [X] have been transmitted by the International Bureau.
   c. [ ] have not been made; however, the time limit for making such amendments has NOT expired.
   d. [ ] have not been made and will not be made.
8. [ ] A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
9. [X] An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)). (unsigned)
10. [ ] A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11. to 16. below concern document(s) or information included:

11. [ ] An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12. [ ] An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. [ ] A FIRST preliminary amendment.
    [ ] A SECOND or SUBSEQUENT preliminary amendment.
14. [ ] A substitute specification.
15. [ ] A change of power of attorney and/or address letter.
16. [X] Other items or information:

Return Postcard
Authorization to Charge Deposit Account

U.S. APPLICATION NO (if known, see 37 CFR 1.5)	INTERNATIONAL APPLICATION NO	ATTORNEY'S DOCKET NUMBER
09/807676	PCT/US99/22940	SOM01 P329A

17. [X] The following fees are submitted:	CALCULATIONS PTO USE ONLY
BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)) :	
Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO **$970.00**	
International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO **$840.00**	
International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO **$690.00**	
International preliminary examination fee paid to USPTO (37 CFR 1.482) but all claims did not satisfy provisions of PCT Article 33(1)-(4) **$670.00**	
International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(1)-(4) **$96.00**	

ENTER APPROPRIATE BASIC FEE AMOUNT =				$	96.00
Surcharge of **$130.00** for furnishing the oath or declaration later than [ ] 20 [ ] 30 months from the earliest claimed priority date (37 CFR 1.492(e)).				$	
CLAIMS	NUMBER FILED		NUMBER EXTRA	RATE	
Total claims	62	- 20 =	42	X **$18.00**	$ 756.00
Independent claims	4	- 3 =	1	X **$78.00**	$ 80.00
MULTIPLE DEPENDENT CLAIM(S) (if applicable)				+ **$260.00**	$ 0.00
TOTAL OF ABOVE CALCULATIONS =				$	932.00
Reduction of 1/2 for filing by small entity, if applicable. A Small Entity Statement must also by filed (Note 37 CFR 1.9, 1.27, 1.28).				$	0.00
SUBTOTAL =				$	932.00
Processing fee of **$130.00** for furnishing the English translation later than [ ]20 [ ] 30 months from the earliest claimed priority date (37 CFR 1.492(f)). +				$	
TOTAL NATIONAL FEE =				$	932.00
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). **$40.00** per property +				$	0.00
TOTAL FEES ENCLOSED =				$	932.00
				Amount to be refunded:	$
				charged:	$

a. [X] A check in the amount of $ 932.00 to cover the above fees is enclosed.

b. [ ] Please charge my Deposit Account No. _____ in the amount of $_____ to cover the above fees. A duplicate copy of this sheet is enclosed.

c. [X] The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 16-2463. A duplicate copy of this sheet is enclosed.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

William W. DeWitt
Price, Heneveld, Cooper, DeWitt & Litton
695 Kenmoor SE
Post Office Box
Grand Rapids, MI 49501
USA

Marcus P. Dolce
SIGNATURE

Marcus P. Dolce
NAME

46 073
REGISTRATION NUMBER

MULTI-CHANNEL NON-INVASIVE TISSUE OXIMETER

This invention relates generally to *in vivo* spectrophotometric examination and monitoring of selected blood metabolites or constituents in human and/or other living subjects, *e.g.*, medical patients, and more particularly to spectrophotometric oximetry, by transmitting selected wavelengths (spectra) of light into a given area of the test subject, receiving the resulting light as it leaves the subject at predetermined locations, and analyzing the received light to determine the desired constituent data based on the spectral absorption which has occurred, from which metabolic information such as blood oxygen saturation may be computed for the particular volume of tissue through which the light spectra have passed.

A considerable amount of scientific data and writings, as well as prior patents, now exist which is/are based on research and clinical studies done in the above-noted area of investigation, validating the underlying technology and describing or commenting on various attributes and proposed or actual applications of such technology. One such application and field of use is the widespread clinical usage of pulse oximeters as of the present point in time, which typically utilize sensors applied to body extremities such as fingers, toes, earlobes, *etc.*, where arterial vasculature is in close proximity, from which arterial hemoglobin oxygenation may be determined non-invasively. A further and important extension of such technology is disclosed and discussed in U.S. Patent No. 5,902,235, which is related to and commonly owned with the present application and directed to a non-invasive spectrophotometric cerebral oximeter, by which blood oxygen saturation in the brain may be non-invasively determined through the use of an optical sensor having light emitters and detectors that is applied to the forehead of the patient. Earlier patents commonly owned with the '235 patent and the present one pertaining to various attributes of and applications for the underlying technology include Nos. 5,139,025; 5,217,013; 5,465,714; 5,482,034; and 5,584,296.

The cerebral oximeter of the aforementioned '235 patent has proved to be an effective and highly desirable clinical instrument, since it provides uniquely important medical information with respect to brain condition (hemoglobin oxygen saturation within the brain, which is directly indicative of the single most basic and important life parameter, *i.e.* brain vitality). This information was not previously available, despite its great importance, since there really is no detectable arterial pulse within brain tissue itself with respect to which pulse oximetry could be utilized even if it could be

effectively utilized in such an interior location (which is very doubtful), and this determination therefore requires a substantially different kind of apparatus and determination analysis. In addition, there are a number of uniquely complicating factors, including the fact that there is both arterial and venous vasculature present in the skin and underlying tissue through which the examining light spectra must pass during both entry to and exit from the brain, and this would distort and/or obscure the brain examination data if excluded in some way. Furthermore, the overall blood supply within the skull and the brain itself consists of a composite of arterial, venous, and capillary blood, as well as some pooled blood, and each of these are differently oxygenated. In addition, the absorption and scatter effects on the examination light spectra are much greater in the brain and its environment than in ordinary tissue, and this tends to result in extremely low-level electrical signal outputs from the detectors for analysis, producing difficult signal-to-noise problems.

Notwithstanding these and other such problems, the cerebral oximeter embodying the technology of the aforementioned issued patents (now available commercially from Somanetics Corporation, of Troy, Michigan) has provided a new type of clinical instrument by which new information has been gained relative to the operation and functioning of the human brain, particularly during surgical procedures and/or injury or trauma, and this has yielded greater insight into the functioning and state of the brain during such conditions. This insight and knowledge has greatly assisted surgeons performing such relatively extreme procedures as carotid endarterectomy, brain surgery, and other complex procedures, including open-heart surgery, *etc.* and has led to a greater understanding and awareness of conditions and effects attributable to the hemispheric structure of the human brain, including the functional inter-relationship of the two cerebral hemispheres, which are subtly interconnected from the standpoint of blood perfusion as well as that of electrical impulses and impulse transfer.

BRIEF SUMMARY OF INVENTION

The present invention results from the new insights into and increased understanding of the human brain referred to in the preceding paragraph, and provides a methodology and apparatus for separately (and preferably simultaneously) sensing and quantitatively determining brain oxygenation at a plurality of specifically different locations or regions of the brain, particularly during surgical or other such traumatic conditions, and visually displaying such determinations in a directly comparative

manner. In a larger sense, the invention may also be used to monitor oxygenation (or other such metabolite concentrations or parameters) in other organs or at other body locations, where mere arterial pulse oximetry is a far too general and imprecise examination technique.

Further, and of considerable moment, the invention provides a method and apparatus for making and displaying determinations of internal metabolic substance, as referred to in the preceding paragraph, at a plurality of particular and differing sites, and doing so on a substantially simultaneous and continuing basis, as well as displaying the determinations for each such site in a directly comparative manner, for immediate assessment by the surgeon or other attending clinician, on a real-time basis, for direct support and guidance during surgery or other such course of treatment.

In a more particular sense, the invention provides a method and apparatus for spectrophotometric *in vivo* monitoring of blood metabolites such as hemoglobin oxygen concentration in any of a preselected plurality of different regions of the same test subject and on a continuing and substantially instantaneous basis, by applying a plurality of spectrophotometric sensors. In a more particular sense, the invention provides a method and apparatus for spectrophotometric *in vivo* monitoring of blood metabolites such as hemoglobin oxygen concentration in any of a preselected plurality of different regions of the same test subject and on a continuing and substantially instantaneous basis, by applying a plurality of spectrophotometric sensors to the test subject at each of a corresponding plurality of testing sites, coupling each such sensor to a control and processing station, operating each such sensor to spectrophotometrically irradiate a particular region within the test subject associated with that sensor, detecting and receiving the light energy resulting from such spectrophotometric irradiation for each such region, conveying signals corresponding to the light energy so received to the control and processing station, analyzing the conveyed signals to determine preselected blood metabolite data, and displaying the data so obtained from each of a plurality of such testing sites and for each of a plurality of such regions, in a region-comparative manner.

The foregoing principal aspects and features of the invention will become better understood upon review of the ensuing specification and the attached drawings, describing and illustrating preferred embodiments of the invention.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 is a pictorial representation of a patient on whom apparatus in accordance with the invention is being used;

Fig. 2 is a fragmentary plan view of a typical sensor used in accordance with the invention;

Fig. 3 is an enlarged, fragmentary, pictorial cross-sectional view of a human cranium, showing the sensors of Fig. 2 applied and in place, generally illustrating both structural and functional aspects of the invention;

Fig. 4 is a front view of a typical control and processing unit for use in the invention, illustrating a preferred display of data determined in accordance with the invention;

Figs. 5, 6, and 7 are graphs representing data displays obtained in accordance with the invention which represent actual surgical procedure results from actual patients;

Fig. 8 is a pictorialized cross-sectional view representing a test subject on which a multiplicity of sensors are placed in sequence, further illustrating the multi-channel capability of the present invention;

Fig. 9 is a schematic block diagram generally illustrating the componentry and system organization representative of a typical implementation of the invention; and

Fig. 10 is a pictorialized cross-sectional view similar to Fig. 8, but still further illustrating the multi-channel capability of the present invention.

DESCRIPTION OF PREFERRED EMBODIMENT

Fig. 1 depicts an illustrative patient 10 on whom an instrument 12 in accordance with the present invention is being employed. As illustrated, the forehead 14 of patient 10 has a pair of sensors 16, 116 secured to it in a bilateral configuration, *i.e.*, one such sensor on each side of the forehead, where each may monitor a different brain hemisphere. Each of the sensors 16, 116 is connected to a processor and display unit 20 which provides a central control and processing station (sometimes hereinafter, referred to as the "oximeter") by a corresponding electrical cable 16A, 116A, which join one another at a dual-channel coupler/pre-amp 18, 118 and then (preferably) proceed to the control and processor 20 as an integrated, multiple-conductor cable 22. As will be understood, the electrical cables just noted include individual conductors for energizing light emitters and operating the related light detectors contained in sensors 16, 116, all as referred to further hereinafter and explained in detail in the various prior patents.

The general nature of a typical structure and arrangement for the sensors 16,116 (which are identical in nature and which may if desired be incorporated into a single physical unit) is illustrated in Fig. 2, and comprises the subject matter of certain of the earlier patents, in particular Nos. 5,465,714; 5,482,034; 5,584,296; and 5,795,292, wherein the structure and componentry of preferred sensors are set forth in detail. For present purposes, it is sufficient to note that the sensors 16, 116 include an electrically actuated light source 24 for emitting the selected examination spectra (*e.g.*, two or more narrow-bandwidth LEDs, whose center output wavelengths correspond to the selected examination spectra), together with a pair of light detectors 26, 28 (*e.g.*, photodiodes) which are preferably located at selected and mutually different distances from the source 24. These electro-optical (*i.e.*, "optode") components are precisely positioned upon and secured to, or within, a sensor body having a foam or other such soft and conformable outer layer which is adhesively secured to the forehead (or other desired anatomical portion) of the patient 10, as generally illustrated in Fig. 1, and individual electrical conductors in cables 16A, 116A provide operating power to the sources 24 while others carry output signals from the detectors 26, 28, which are representative of detected light intensities received at the respective detector locations and must be conveyed to the processor unit 20, where processing takes place.

Figure 3 generally illustrates, by way of a pictorialized cross-sectional view, the sensors 16, 116 in place upon the forehead 14 of the patient 12. As illustrated in this figure, the cranial structure of patient 12 generally comprises an outer layer of skin 30, an inner layer of tissue 32, and the frontal shell 34 of the skull, which is of course bone. Inside the skull 34 is the Periosteal Dura Mater, designated by the numeral 36, and inside that is the brain tissue 38 itself, which is comprised of two distinct hemispheres 38′, 38′′ that are separated at the center of the forehead inwardly of the superior sagital sinus by a thin, inwardly-projecting portion 36a of the Dura 36. Thus, in the arrangement illustrated in Fig. 3, sensor 16 accesses and examines brain hemisphere 38′′, while sensor 116 does the same to brain hemisphere 38′.

As explained at length in various of the above-identified prior patents, the preferred configuration of sensors 16, 116 includes both a "near" detector 26, which principally receives light from source 24 whose mean path length is primarily confined to the layers of skin, tissue, skull, *etc.*, outside brain 38, and a "far" detector 28, which receives light spectra that have followed a longer mean path length and traversed a

substantial amount of brain tissue in addition to the bone and tissue traversed by the "near" detector 26. Accordingly, by appropriately differentiating the information from the "near" (or "shallow") detector 26 (which may be considered a first data set) from information obtained from the "far" (or "deep") detector 28 (providing a second such data set), a resultant may be obtained which principally characterizes conditions within the brain tissue itself, without effects attributable to the overlying adjacent tissue, *etc.* This enables the apparatus to obtain metabolic information on a selective basis, for particular regions within the test subject, and by spectral analysis of this resultant information, employing appropriate extinction coefficients, *etc.* (as set forth in certain of the above-identified patents), a numerical value, or relative quantified value, may be obtained which characterizes metabolites or other metabolic data (*e.g.*, the hemoglobin oxygen saturation) within only the particular region or volume of tissue actually examined, *i.e.*, the region or zone generally defined by the curved mean path extending from source 24 to the "far" or "deep" detector 28, and between this path and the outer periphery of the test subject but excluding the analogous region or zone defined by the mean path extending from source 24 to "near" detector 26. As will be understood, particularly in view of Applicant's above-identified prior patents as well as is explained further hereinafter, this data analysis carried out by the "control and processing unit" 20 is accomplished by use if an appropriately programmed digital computer, as is now known by those skilled in the art (exemplified in particular by the Somanetics® model 4100 cerebral oximeter).

The present invention takes advantage of the primarily regional oxygen saturation value produced by each of the two (or more) sensors 16, 116, together with the natural hemispheric structure of brain 38, by use of a comparative dual or other multi-channel examination paradigm that in the preferred embodiment or principal example set forth herein provides a separate but preferably comparatively displayed oxygen saturation value for each of the two brain hemispheres 38′, 38′′. Of course, it will be understood that each such regional index or value of oxygen saturation is actually representative of the particular region within a hemisphere actually subjected to the examining light spectra, and while each such regional value may reasonably be assumed to be generally representative of the entire brain hemisphere in which it is located, and therefor useful in showing and contrasting the differing conditions between the two such hemispheres of the brain 38, the specific nature and understanding of these hemispheric

interrelationships and of interrelationships between other and different possible sensor locations relative to each different hemisphere 38′, 38′′ are not believed to be fully known and appreciated as of yet. Consequently, it may be useful or advantageous in at least some cases, and perhaps in many, to employ a more extensive distribution and array of sensors and corresponding inputs to the oximeter 20, such as is illustrated for example in Figure 8.

Thus, as seen in Fig. 8, a more extensive array of sensors 16, 116, 216, *etc.*, may be deployed around the entire circumference of the head or other such patient extremity, for example, each such sensor sampling a different regional area of each brain hemisphere or other such organ or test site and outputting corresponding data which may be contrasted in various ways with the analogous data obtained from the other such sensors for other test site regions. In this regard, it will be appreciated that the extent of each such regional area subjected to examination is a function of a number of different factors, particularly including the distance between the emitter or source 24 and detectors 26, 28 of each such set and the amount of light intensity which is utilized, the greater the emitter/sensor distance and corresponding light intensity, the greater the area effectively traversed by the examining light spectra and the larger the size of the "region" whose oximetric or other metabolic value is being determined.

It may also be possible to use only a single source position and employ a series of mutually spaced detector sets, or individual detectors, disposed at various selected distances from the single source around all or a portion of the perimeter of the subject. Each such single source would actually illuminate the entire brain since the photons so introduced would scatter throughout the interior of the skull (even though being subject to increased absorption as a function of distance traversed), and each such emitter/detector pair (including long-range pairs) could produce information characterizing deeper interior regions than is true of the arrays illustrated in Figs. 3 and 8, for example. Of course, the smaller-region arrays shown in these figures are desirable in many instances, for a number of reasons. For example, the comparative analysis of information corresponding to a number of differing such regions, as represented by the array of Figure 8, lends itself readily to very meaningful comparative displays, including for example computer-produced mapping displays which (preferably by use of differing colors and a color monitor screen) could be used to present an ongoing real-time model which would illustrate blood or even tissue oxygenation state

around the inside perimeter of and for an appreciable distance within a given anatomical area or part. The multiple detector outputs from such a single-source arrangement, on the other hand, would contain information relative to regions or areas deep within the brain, and might enable the determination of rSO_2 values (or other parameters) for deep internal regions as well as the production of whole-brain mapping, by differentially or additively combining the outputs from various selected detectors located at particular points.

The dual or bilateral examination arrangement depicted in Figs. 1 and 3 will provide the highly useful comparative display formats illustrated in Figs. 4, 5, 6, and 7 (as well as on the face of the oximeter 20 shown at the right in Fig. 1), for example. In the arrangement shown in Figs. 1 and 4, each sensor output is separately processed to provide a particular regional oxygen saturation value, and these regional values are separately displayed on a video screen 40 as both a numeric or other such quantified value, constituting a basically instantaneous real-time value, and as a point in a graphical plot 42, 44, representing a succession of such values taken over time. As illustrated, the plots or graphs 42, 44 may advantageously be disposed one above the other in direct alignment, for convenient examination and comparison. While the instantaneous numeric displays will almost always be found useful and desirable, particularly when arranged in the directly adjacent and immediately comparable manner illustrated, the graphical trace displays 42, 44 directly show the ongoing trend, and do so in a contrasting, comparative manner, as well as showing the actual or relative values, and thus are also highly useful.

Graphic displays 42, 44 may also advantageously be arranged in the form shown in Figs. 5, 6, and 7, in which the two such individual traces are directly superimposed upon one another, for more immediate and readily apparent comparison and contrast. Each of the examples shown in Figs. 5, 6, and 7 does in fact represent the record from an actual surgical procedure in which the present invention was utilized, and in each of these the vertical axis (labeled rSO_2) is indicative of regional oxygen saturation values which have been determined, while the horizontal axis is, as labeled, "real time," *i.e.*, ongoing clock time during the surgical procedure involved. The trace from the "left" sensor (number 16 as shown in Figs. 1 and 3), designated by the numeral 42 for convenience, is shown in solid lines in these graphs, whereas the trace 44 from the right-hand sensor 116 is shown in dashed lines. The sensors may be placed on any region of

their respective test areas (*e.g.*, brain hemispheres) provided that any underlying hair is first removed, since hair is basically opaque to the applied light spectra and thus greatly reduces the amount of light energy actually introduced to the underlying tissue, *etc.*

With further reference to Figs. 5, 6, and 7, and also inferentially to Fig. 4, it will be seen that at certain times, (*e.g.*, the beginning and end of each procedure, when the patient's condition is at least relatively normal) there is a certain amount of direct correspondence between the two different hemispheric traces 42, 44, and that in at least these time increments the shape of the two traces is reasonably symmetrical and convergent. An idealized such normal result is shown in Fig. 1, wherein both the numeric values and the curves are basically the same. In each of the procedures shown in Figs. 5, 6, and 7, however, there are times when the detected regional cerebral oxygen saturation differs markedly from one brain hemisphere to the other. This is particularly noticeable in Fig. 6, in which it may be observed that the left hand trace 42 is at times only about one half the height (*i.e.*, value) of the right hand trace 44, reaching a minimal value in the neighborhood of about 35% slightly before real time point 12:21 as compared to the initial level, at time 10:50-11:00, of more than 75%, which is approximately the level of saturation in the right hemisphere at the 12:21 time just noted, when the oxygenation of the left hemisphere had decreased to approximately 35%.

As will be understood, the various differences in cerebral blood oxygenation shown by the superimposed traces of Figs. 5, 6, and 7 occur as a result of measures taken during the corresponding surgical procedures, which in these cases are carotid endarterectomies and/or coronary artery bypass graft (CABG), which are sometimes undertaken as a continuing sequence. In the illustrated examples, Figure 5 represents a sequential carotid endarterectomy and hypothermic CABG, in which the vertical lines along the time axis characterize certain events during surgery, *i.e.*, index line 46 represents the time of the carotid arterial incision, line 48 represent the time the arterial clamp was applied and the shunt opened (resulting in reduced arterial blood flow to the left brain hemisphere), index line 50 represents a time shortly after the shunt was removed and the clamp taken off, and the area from about real time 17:43 to the end of the graph was when the hypothermic brain surgery actually took place, the lowest point (just prior to time 18:23) occurring when the heart-lung machine pump was turned on, and the indices at time 19:43 and 20:23 generally show the time for blood rewarming and pump off, respectively. While illustrative and perhaps enlightening, it is not considered

necessary to give the specifics of the surgical procedures portrayed by the graphical presentations of Figs. 6 and 7, although it may be noted that the procedure of Fig. 6 was a carotid endarterectomy of the left side and that of Fig. 7 was a similar endarterectomy on the right side of a different patient. Sufficient to say that these graphs represent other such surgical procedures and show comparable states of differing hemispheric oxygenation.

The importance and value of the information provided in accordance with the present invention is believed self-apparent from the foregoing, particularly the graphical presentations of and comments provided with respect to Figs. 5, 6, and 7. Prior to the advent of the present invention, no such comparative or hemispheric-specific information was available to the surgeon, who did not in fact have any quantified or accurately representative data to illustrate the prevailing hemispheric brain oxygenation conditions during a surgery. Thus, even the use of a single such sensor (16, 116) on the side of the brain on which a procedure is to be done is highly useful and, as of the present time, rapidly being recognized as essential. Of course, it is considerably more useful to have at least the bilateral array illustrated in Fig. 1, to provide comparative data such as that seen in Figs. 4-7 inclusive.

Figure 9 is a schematic block diagram generally illustrating the componentry and system organization making up a typical implementation of the invention, as shown pictorially in Fig. 1 (to which reference is also made). As shown in Fig. 9, the oximeter 20 comprises a digital computer 50 which provides a central processing unit, with a processor, data buffers, and timing signal generation for the system, together with a keypad interface (shown along the bottom of the unit 20 in Fig. 1), display generator and display 40 (preferably implemented by use of a flat electro-luminescent unit, at least in applications where a sharp monochromatic display is sufficient), as well as an audible alarm 52 including a speaker, and a data output interface 54 by which the computer may be interconnected to a remote personal computer, disk drive, printer, or the like for downloading data, *etc.*

As also shown in Fig. 9, each of the sensors 16, 116 (and/or others, in the multi-site configuration illustrated in Fig. 8) receives timing signals from the CPU 50 and is coupled to an LED excitation current source (56,156) which drives the emitters 24 of each sensor. The analog output signals from the detectors (photodiodes) 26, 28 of each sensor are conveyed to the coupler/pre-amp 18, 118 for signal conditioning (filtering and

amplification), under the control of additional timing signals from the CPU. Following that, these signals undergo A-to-D conversion and synchronization (for synchronized demodulation, as noted hereinafter), also under the control of timing signals from CPU 50, and they are then coupled to the CPU for computation of regional oxygen saturation rSO_2 data, storage of the computed data, and display thereof, preferably in the format discussed above in conjunction with Figs. 4, 5, 6, and 7. As will be apparent, each sensor (16, 116, *etc.*) preferably has its own signal-processing circuitry (pre-amp, *etc.*) upstream of CPU 50, and each such sensor circuit is preferably the same.

While implementation of a system such as that shown in Fig. 9 is as a general matter well within the general skill of the art once the nature and purpose of the system and the basic requirements of its components, together with the overall operation (as set forth above and hereinafter) have become known, at least certain aspects of the preferred such system implementation are as follows. First, it is preferable that the light emitters 24 (*i.e.*, LEDs) of each of the different sensors 16, 116 *etc.*, be driven out-of-phase, sequentially and alternatingly with one another (*i.e.*, only a single such LED or other emitter being driven during the same time interval, and the emitters on the respective different sensors are alternatingly actuated, so as to ensure that the detectors 26, 28 of the particular sensor 16, 116 then being actuated receive only resultant light spectra emanating from a particular emitter located on that particular sensor, and no cross-talk between sensors takes place (even though significant levels of cross-talk are unlikely in any event due to the substantial attenuation of light intensity as it passes through tissue, which is on the order of about ten times for each centimeter of optical path length through tissue). Further, it is desirable to carefully window the "on" time of the detectors 26, 28 so that each is only active during a selected minor portion (for example, 10% or less) of the time that the related emitter is activated (and, preferably, during the center part of each emitter actuation period). Of course, under computer control such accurate and intricate timing is readily accomplished, and in addition, the overall process may be carried on at a very fast rate.

In a multi-site (multiple sensor) system, such as that shown in Fig. 8, the preferred implementation and system operation would also be in accordance with that shown in Fig. 9, and the foregoing comments regarding system performance, data sampling, *etc.*, would also apply, although there would of course be a greater number of sensors and sensor circuit branches interfacing with computer 50. The same would also

be basically true of a single-source multi-site detector configuration or grouping such as that referred to above, taking into consideration the fact that the detectors would not necessarily be grouped in specific or dedicated "near-far" pairs and bearing in mind that one or more detectors located nearer a source than another detector, or detectors, located further from the source could be paired with or otherwise deemed a "near" detector relative to any such farther detector. In any such multiple-site configuration, it may be advantageous to implement a prioritized sequential emitter actuation and data detection timing format, in which more than one emitter may be operated at the same time, or some particular operational sequence is followed, with appropriate signal timing and buffering, particularly if signal cross-talk is not a matter of serious consideration due to the particular circumstances involved (detector location, size and nature of test subject, physiology, signal strength, *etc.)*. As illustrated in Fig. 10, a multi-sensor or multiple sector-emitter array may be so operated, by using a number of different emitter-detector pair groupings, with some detectors used in conjunction with a series of different emitters to monitor a number of differing internal sectors or regions.

A system as described above may readily be implemented to obtain on the order of about fifteen data samples per second even with the minimal detector "on" time noted, and a further point to note is that the preferred processing involves windowing of the detector "on" time so that data samples are taken alternatingly during times when the emitters are actuated and the ensuing time when they are not actuated (*i.e.*, "dark time"), so that the applicable background signal level may be computed and utilized in analyzing the data taken during the emitter "on" time. Other features of the preferred processing include the taking of a fairly large number (*e.g.*, 50) of data samples during emitter "on" time within a period of not more than about five seconds, and processing that group of signals to obtain an average from which each updated rSO_2 value is computed, whereby the numeric value displayed on the video screen 40 is updated each five seconds (or less). This progression of computed values is preferably stored in computer memory over the entire length of the surgical procedure involved, and used to generate the graphical traces 42, 44 on a time-related basis as discussed above. Preferably, non-volatile memory is utilized so that this data will not be readily lost, and may in fact be downloaded at a convenient time through the data output interface 54 of CPU 50 noted above in connection with Fig. 9.

As will be understood, the foregoing disclosure and attached drawings are directed to a single preferred embodiment of the invention for purposes of illustration; however, it should be understood that variations and modifications of this particular embodiment may well occur to those skilled in the art after considering this disclosure, and that all such variations *etc.*, should be considered an integral part of the underlying invention, especially in regard to particular shapes, configurations, component choices and variations in structural and system features. Accordingly, it is to be understood that the particular components and structures, etc. shown in the drawings and described above are merely for illustrative purposes and should not be used to limit the scope of the invention, which is defined by the following claims as interpreted according to the principles of patent law, including the doctrine of equivalents.

The invention claimed is:

1. A method for spectrophotometric in vivo monitoring and display of blood metabolites in a plurality of different internal regions of the same test subject on a substantially simultaneous basis, comprising the steps of:

applying a plurality of spectrophotometric sensors to a test subject at each of a corresponding plurality of testing sites and coupling each such sensor to a control and processing station;

operating a selected number of said sensors to spectrophotometrically irradiate at least two internal regions of the test subject during a common time interval, each such region being associated with a different such testing site;

separately detecting and receiving the light energy resulting from said spectrophotometric irradiation for each of said two different regions, and conveying separate signals to said control and processing station which correspond to the separately detected light energy;

analyzing said conveyed signals to separately determine quantified data representative of the same blood metabolite in each of said at least two internal regions; and

visually displaying said quantified data for each of said at least two different regions for direct mutual comparison.

2. The method of claim 1, wherein said step of analyzing comprises determination of blood oxygenation level within each of said at least two regions.

3. The method of claim 2, wherein said analyzing step includes producing a separate quantitative value determination for hemoglobin oxygen saturation for each of said at least two different regions.

4. The method of claim 3, wherein said analyzing determination includes production of an ongoing graphical trace representing a plurality of said quantitative value designations made at successive points in time.

5. The method of claim 3 including the step of visually displaying a plurality of said quantitative value designations at substantially the same time and in predetermined relationship to one another to facilitate rapid and accurate visual comparison.

6. The method of claim 4 including the step of visually displaying a plurality of said graphical traces at substantially the same time and in predetermined relationship to one another to facilitate rapid and accurate visual comparison.

7. The method of claim 6 including the step of visually displaying a plurality of said quantitative value designations as well as said graphical traces at substantially the same time and in predetermined relationship to one another to facilitate rapid and accurate visual comparison.

8. The method of claim 1, including the step of providing signals to said control and processing station which comprise at least two data sets that cooperatively define blood metabolite data for a particular area within an individual one of said regions.

9. The method of claim 1, wherein said sensors are applied to the head of the test subject and used to monitor the brain.

10. The method of claim 9, wherein said metabolite comprises hemoglobin oxygen.

11. The method of claim 9, wherein said sensors are positioned in locations proximate to different brain hemispheres and said two internal regions are each located in a different such brain hemisphere.

12. The method of claim 11, wherein said metabolite comprises cerebral blood hemoglobin oxygenation.

13. The method of claim 11, including the step of providing signals to said control and processing station which comprise at least two data sets which cooperatively define blood metabolite data for an individual area within at least one of said particular regions.

14. The method of claim 8, wherein said provided data sets include one such set which characterizes a first zone within one of said regions and another such set which characterizes a second zone that is at least partially within the same said region.

15. The method of claim 14, wherein said second zone characterized by said other such data set includes at least part of said first zone.

16. The method of claim 1, wherein said sensors are applied to the outside periphery of the test subject and operate non-invasively.

17. Apparatus for spectrophotometric in vivo monitoring of blood metabolites in each of a plurality of different internal regions on a substantially concurrent basis, comprising:

a plurality of spectrophotometric sensors, each attachable to a test subject at a different test location and adapted to spectrophotometrically irradiate a given region within the test subject associated with each such test location;

a controller and processor, and circuitry coupling each such sensor to said controller and processor for individually operating certain of said sensors to spectrophotometrically irradiate said given internal region within the test subject associated with each such test location;

said sensors each further adapted to receive light energy resulting from the spectrophotometric irradiation by that sensor of its associated region on a substantially concurrent basis with other such sensors, and to produce separate signals corresponding to the light energy so received; and said circuitry acting to convey said separate signals to said controller and processor for separate analytic processing;

said controller and processor adapted to analytically process said conveyed signals separately and thereby determine separate quantified blood metabolite data therefrom for separate such sensors; and

a visual display coupled to said controller and processor and adapted to separately display the quantified metabolite data so determined for each of a plurality of sensors in a mutually-comparative manner.

18. The apparatus of claim 17, wherein said controller and processor is adapted to analyze said data to determine blood oxygenation within at least two separate internal regions.

19. The apparatus of claim 18, wherein said controller and processor is adapted to produce numeric value designations for hemoglobin oxygen saturation for at least two of said regions.

20. The apparatus of claim 19, wherein said controller and processor and said display are adapted to produce an ongoing graphical trace representing a plurality of said numeric value designations for the same region taken over a period of time.

21. The apparatus of claim 19 wherein said controller and processor and said display are adapted to visually display at least two of said numeric value designations on a substantially concurrent basis and in predetermined relationship to one another to facilitate rapid and accurate visual comparison.

22. The apparatus of claim 20 wherein said controller and processor and said display are adapted to visually display at least two of said graphical traces on a substantially concurrent basis and in predetermined relationship to one another to facilitate rapid and accurate visual comparison.

23. The apparatus of claim 22 wherein said controller and processor and said display are adapted to visually display at least two of said numeric value designations as well as at least two of said graphical traces on a substantially concurrent basis and in proximity to one another to facilitate rapid and accurate visual comparison.

24. The apparatus of claim 17, wherein said sensors are adapted to provide signals to said controller and processor which comprise at least two separate data sets that cooperatively define at least portions of a particular area within a given such region.

25. The apparatus of claim 17, wherein said sensors are adapted to be applied to the head of a test subject and to monitor its brain.

26. The apparatus of claim 25, wherein said computer is adapted to determine blood oxygenation saturation in said brain.

27. The apparatus of claim 25, wherein said sensors are adapted to be positioned in locations associated with different hemispheres of the same brain and are operable to separately monitor at least portions of each such different hemisphere.

28. The apparatus of claim 27, wherein said controller and processor is adapted to determine cerebral blood oxygenation saturation within said two different brain hemispheres.

29. The apparatus of claim 27, wherein said sensors are adapted to provide signals to said controller and processor which comprise at least two data sets that cooperatively define at least portions of a particular area within the same such internal regions.

30. The apparatus of claim 24, wherein said data sets provided by said sensors include one such set characterizing a first zone adjacent said given region and another such set characterizing a second zone at least partially within said given region.

31. The apparatus of claim 30, wherein said second zone characterized by said other such data set includes at least part of said first zone.

32. The apparatus of claim 17, wherein said sensors are adapted to be applied to the outside periphery of the test subject and to operate non-invasively.

33. A method for substantially simultaneous comparative in vivo monitoring of blood metabolites in each of a plurality of different internal regions of at least one selected test subject, comprising the steps of:

spectrophotometrically irradiating each of a plurality of different testing sites on said at least one test subject;

detecting light energy resulting from said spectrophotometric irradiation for a plurality of such testing sites, and providing signals to a control and processing station which are representative of the light energy so received for said plurality of testing sites;

analyzing said conveyed signals to determine quantified blood metabolite data representative of at least one defined region within said at least one test subject associated with each of at least two different such testing sites, each such defined region being different from the other; and

displaying said data for each of said at least two different regions at substantially the same time for direct mutual comparison.

34. The method of claim 33, wherein the step of providing signals to said control and processing station comprises providing at least two data sets that cooperatively define blood metabolite data for an individual one of said defined regions.

35. The method of claim 34, wherein said provided data sets include one such set which characterizes a first zone proximate to said defined region and another such set which characterizes a second zone that is at least partially within said defined region.

36. The method of claim 35, wherein said second zone characterized by said other such data set includes at least part of said first zone.

37. The method of claim 33, wherein said step of spectrophotometrically irradiating is carried out by using a plurality of sensors applied to the outside periphery of the test subject and operated non-invasively.

38. The method of claim 33, wherein said control and processing station is used to time and sequence emission of spectrophotometric radiation and detection of resulting light energy by said sensors.

39. The method of claim 33, wherein said spectrophotometric irradiation by said sensors is done sequentially and alternatively.

40. The method of claim 33, wherein said spectrophotometric irradiation comprises application of at least two different wavelengths, and such wavelengths are applied in an alternating sequence of timed pulses.

41. The method of claim 40, including detection of the resulting light energy corresponding to each of said wavelengths on a timed periodic basis using periods whose occurrence generally corresponds to that of said applied spectrophotometric wavelength pulses.

42. The method of claim 41, wherein the duration of each of said timed detection periods is limited to a length which is less than that of each pulse of applied spectrophotometric irradiation energy.

43. The method of claim 42, wherein the duration of each of said detection periods is less than half that of a pulse of said applied spectrophotometric irradiation.

44. The method of claim 43, wherein a plurality of said detection periods are used during pulses of said applied irradiation, and a corresponding energy detection occurs during each of a plurality of said detection periods.

45. The method of claim 44, further including the steps of averaging a selected number of energy detection event values to obtain a resultant value therefor, and using said resultant value to compute a metabolite value which is representative thereof.

46. The method of claim 45, wherein said display includes said computed representative metabolite value.

47. The method of claim 46, wherein said display is refreshed periodically by using a sequence of computed representative metabolite values which are based upon and represent the averaged detection event values produced during the different time intervals corresponding to the intervals of said periodic display refreshment.

48. Apparatus for spectrophotometric in vivo monitoring of a selected metabolic condition in each of a plurality of different test subject regions on a substantially concurrent basis, comprising:

a plurality of spectrophotometric emitters, each adapted to spectrophotometrically irradiate a designated region within a test subject from a test location on such test subject;

a controller and processor, and circuitry coupling each such emitter to said controller and processor for individually operating selected such emitters to spectrophotometrically irradiate at least two regions within a test subject from at least one selected test location;

a plurality of detectors adapted to receive light energy resulting from the spectrophotometric irradiation of said at least two regions, and to produce at least one separate set of corresponding signals for each such region; and circuitry acting to convey said separate sets of signals to said controller and processor for analytic processing;

said controller and processor adapted to analytically process said conveyed sets of signals to determine separate sets of quantified data representative of said metabolic condition in said at least two regions; and

a visual display coupled to said controller and processor and adapted to display separate representations of said separate sets of quantified metabolic data for said at least two regions in a mutually-comparative manner and on a substantially simultaneous basis.

49. The apparatus of claim 48, wherein said controller and processor includes a computer programmed to analyze said detector signals to determine the blood oxygenation state within each of said at least two regions.

50. The apparatus of claim 49, wherein said computer comprises a processor, data buffers, and a timing signal generator, said data buffers adapted to store data representative of said blood oxygenation state and said timing signal generator adapted to control actuation of said emitters and detectors accordingly.

51. The apparatus of claim 49, wherein said controller and processor comprises a unitary device which includes said computer and said display.

52. The apparatus of claim 51 wherein said unitary controller and processor device further includes a keyboard interface to said computer.

53. The apparatus of claim 51 wherein said unitary controller and processor device further includes a data output interface.

54. The apparatus of claim 53 wherein said unitary controller and processor device further includes an integral keyboard interface to said computer.

55. The apparatus of claim 51, wherein said display comprises a flat electroluminescent visual display screen.

56. The apparatus of claim 55 wherein said unitary controller and processor unit further includes an integral keyboard interface to said computer.

57. The apparatus of claim 48, wherein at least certain of said detectors and certain of said emitters comprise operational pairs, and said controller and processor is arranged to operate the emitters and detectors of at least certain of such pairs in predetermined timed relationship while maintaining the emitters and detectors of other such pairs in a non-operating condition.

58. The apparatus of claim 57, wherein said controller and processor is adapted to sequence the operation of certain of such emitter-detector pairs.

59. The apparatus of claim 57, wherein at least certain of said operational emitter detector pairs include at least two detectors and at least one such detector is located nearer the emitter of such pair than at least one of the other detectors to provide near and far detector groupings for that operational pair.

60. The apparatus of claim 58, wherein at least certain of said operational pairs include a plurality of said detectors arranged at mutually spaced locations which are spaced at differing distances from the emitter of their operational pair.

61. The apparatus of claim 59, wherein said controller and processor is adapted to sequence the operation of certain of such emitter-detector pairs.

62. The apparatus of claim 60, wherein said controller and processor is adapted to operate the emitter and a selected number less than all of the detectors of at least one of said at least certain of said operational pairs substantially in unison while holding the other detectors of said at least one operational pair in non-operating condition, and said controller and processor is further arranged to operate such other detectors substantially in unison with said emitter at another time during which said selected number of detectors are maintained in a non-operating condition.

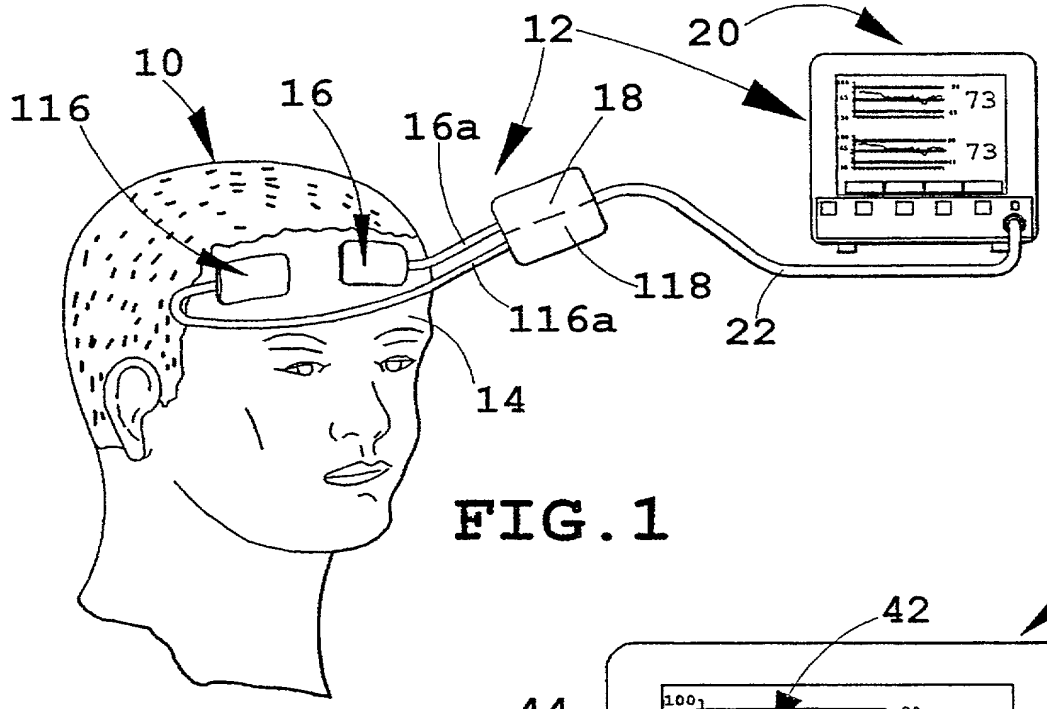

FIG. 1

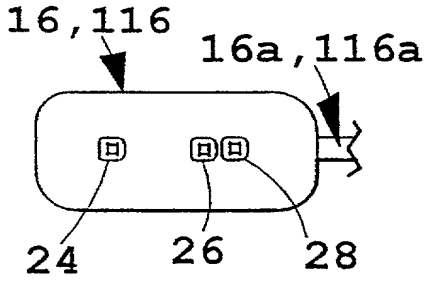

FIG. 2

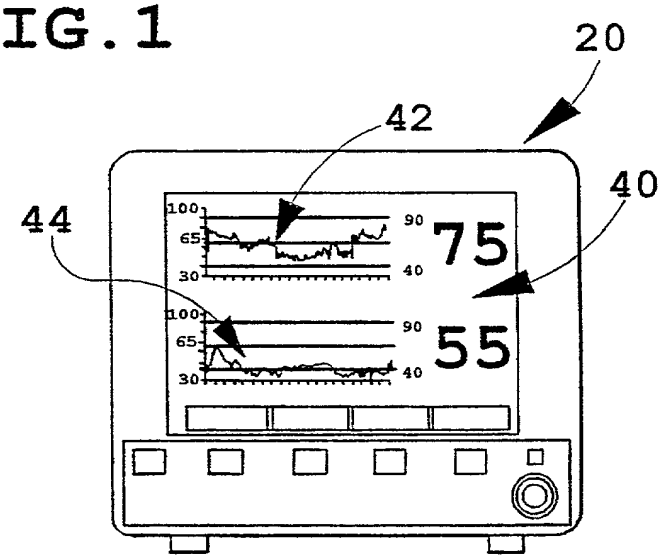

FIG. 4

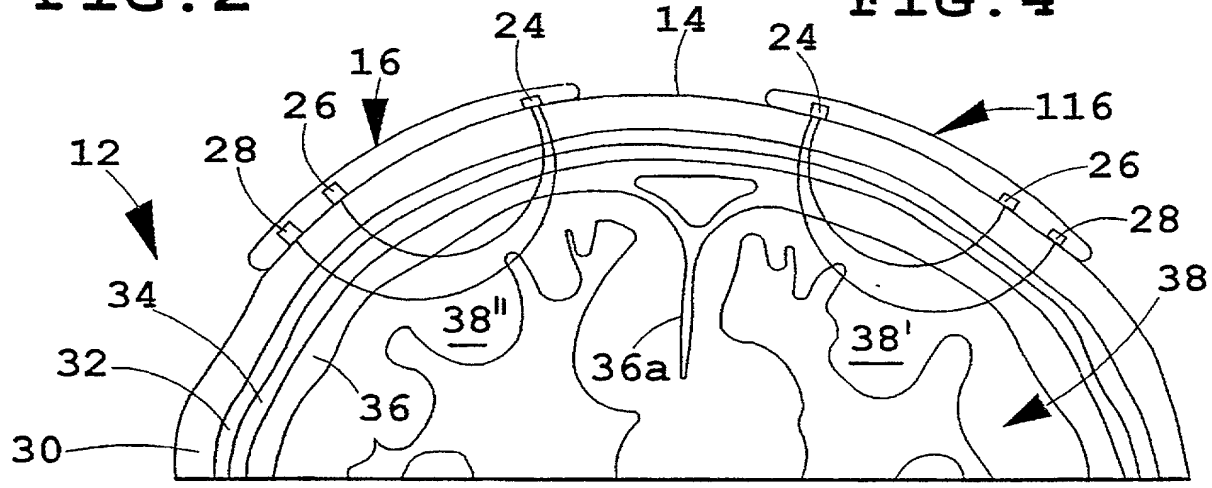

FIG. 3

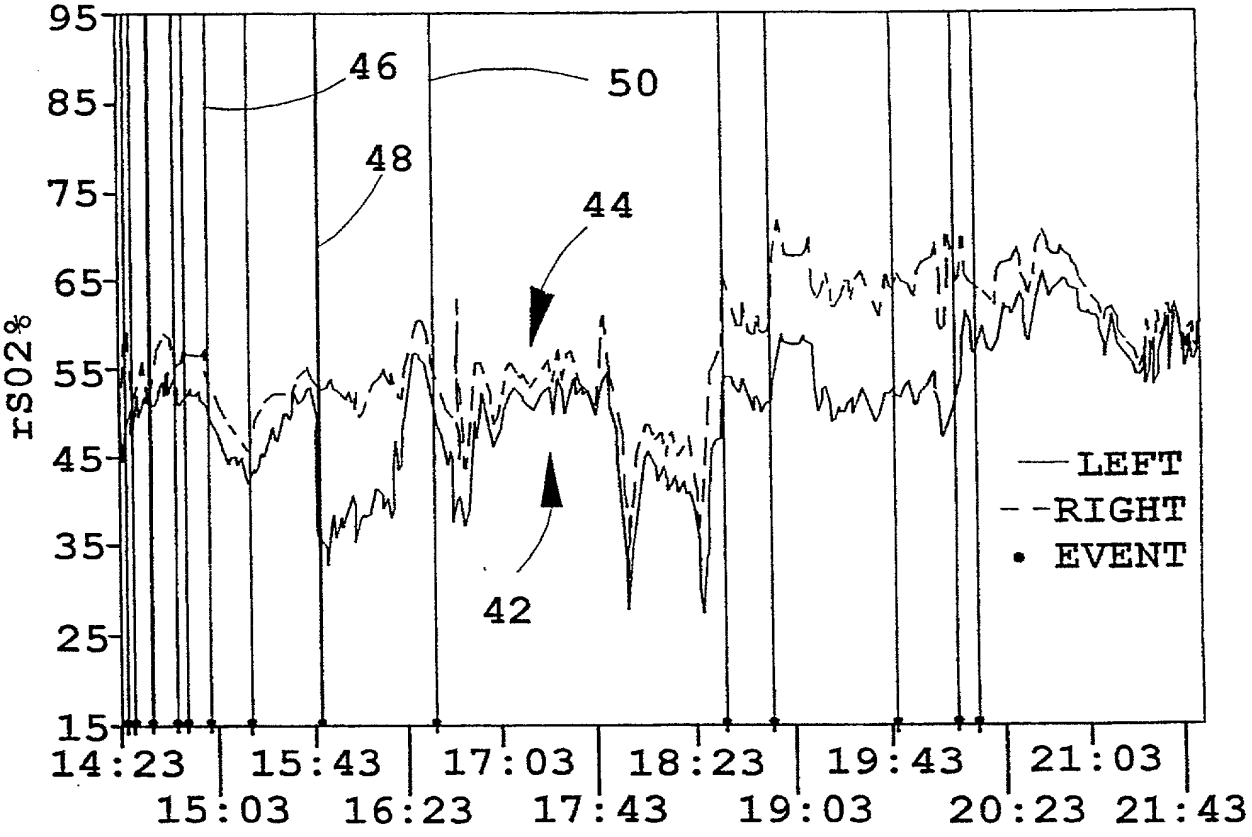

FIG. 5

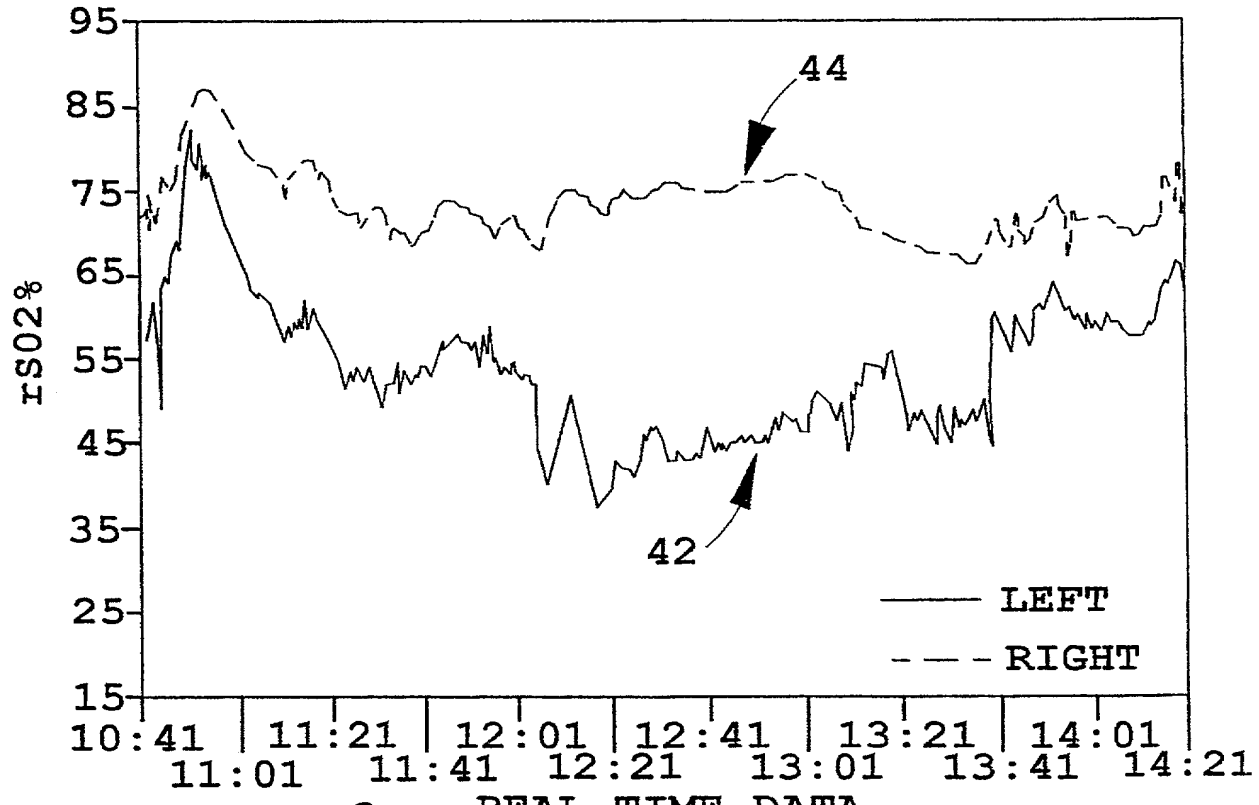

FIG. 6

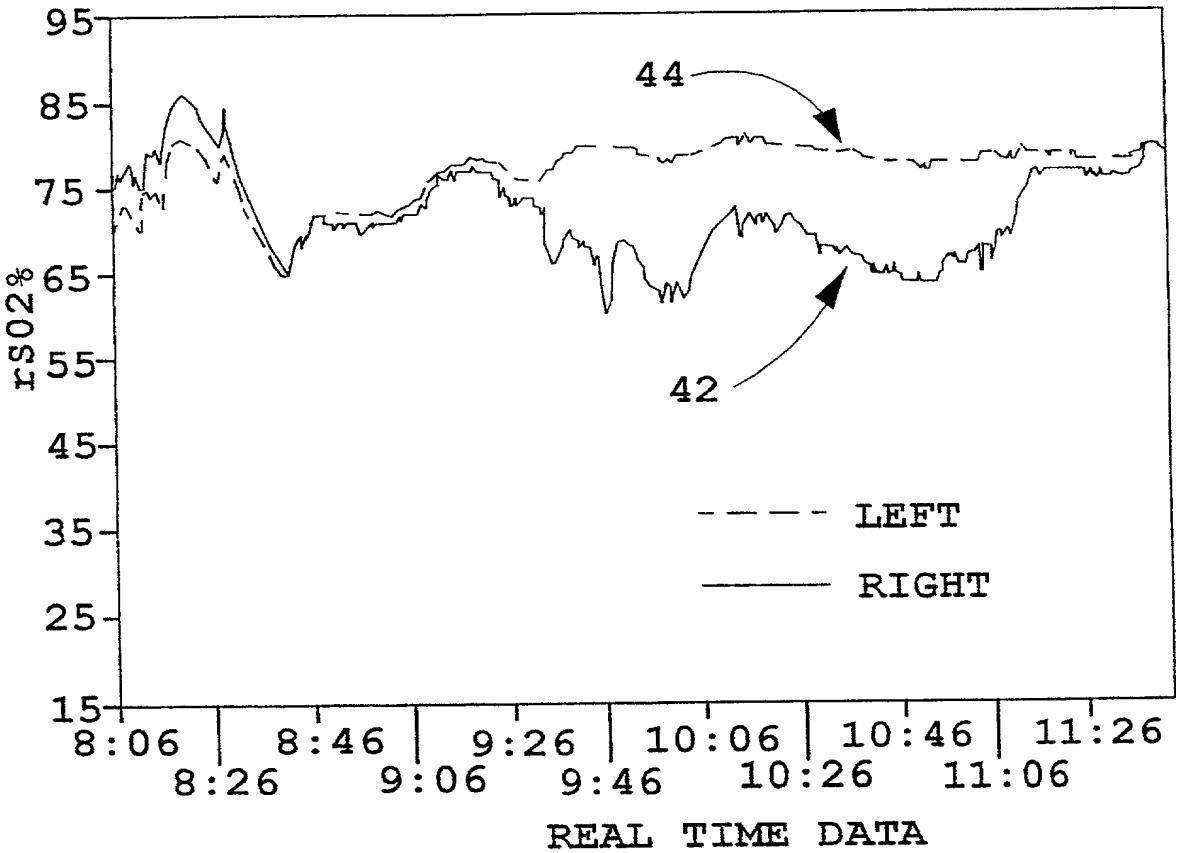

FIG. 7

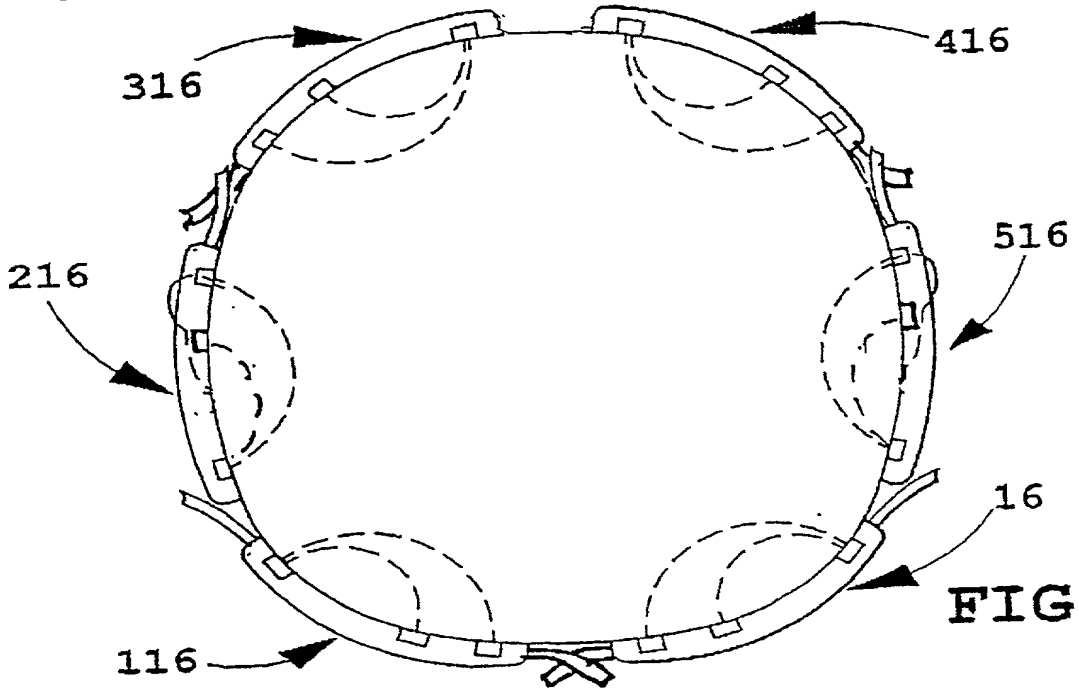

FIG. 8

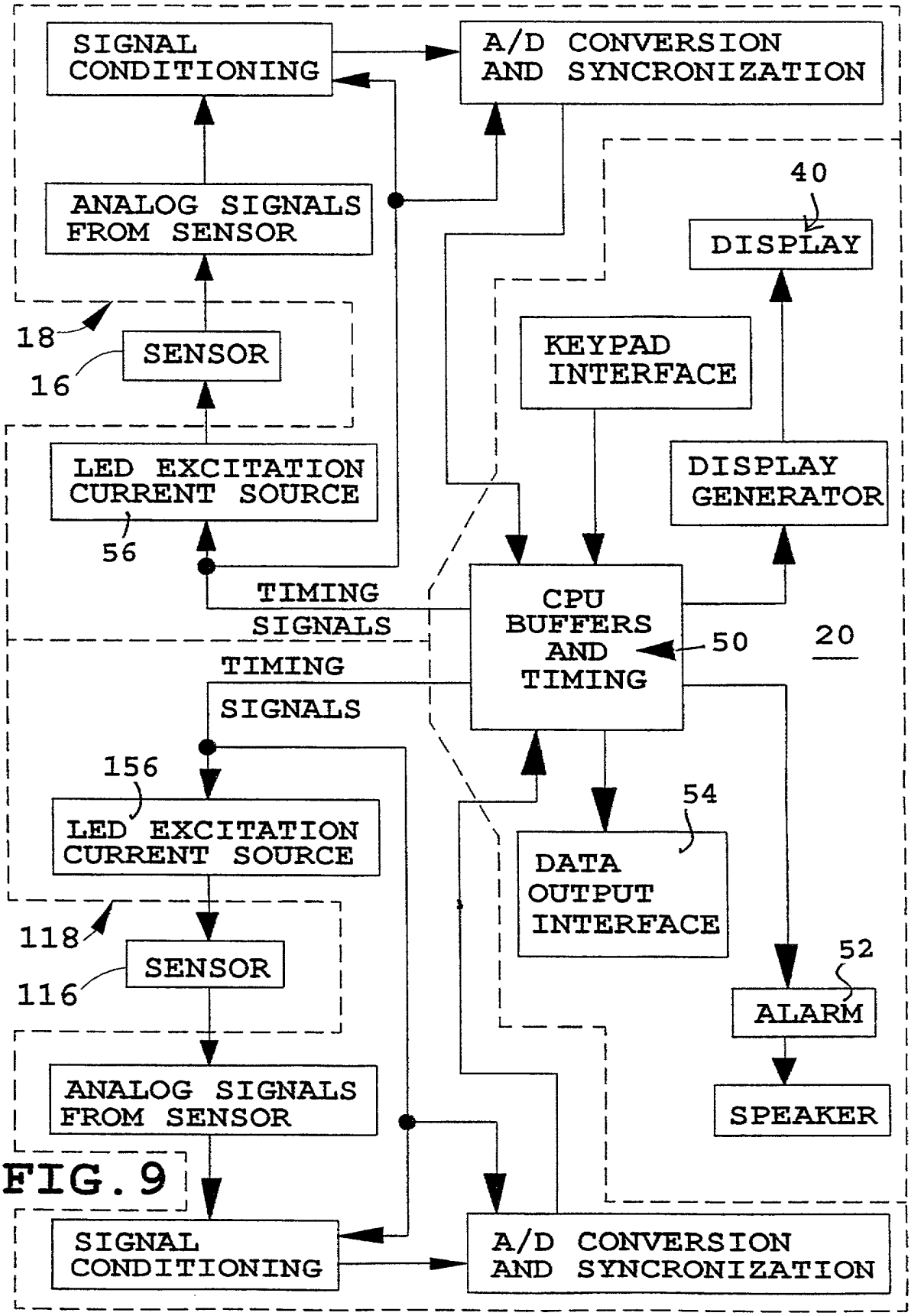

FIG. 9

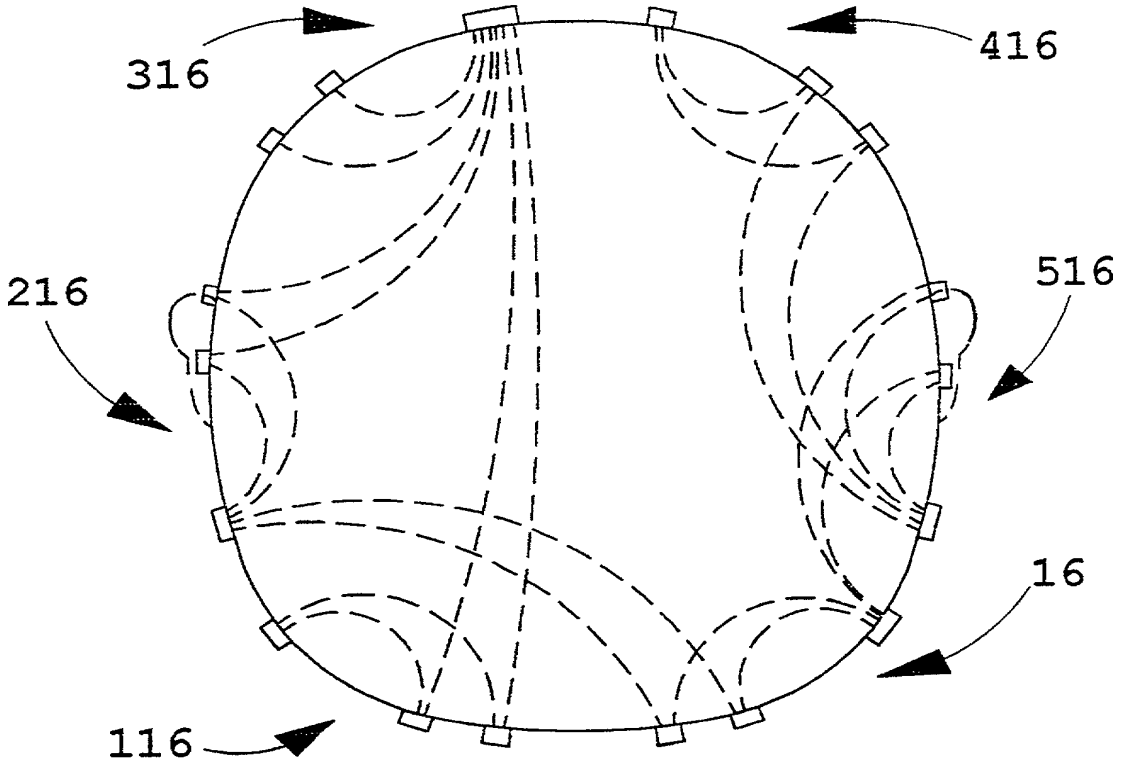

FIG.10

Atty. Docket No. SOM01 P329A

DECLARATION AND POWER OF ATTORNEY

As a below named inventor, I hereby declare:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am an original, first and joint inventor, if plural names are listed below, of the subject matter which is claimed and for which a patent is sought on the invention entitled **MULTI-CHANNEL NON-INVASIVE TISSUE OXIMETER**, the specification of which was filed on April 13, 2001 and assigned Application No. 09/807,676.

I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose to the United States Patent and Trademark Office (the Office), all information which is known by me to be material to patentability as defined in Title 37, Code of Federal Regulations (C.F.R.), Section 1.56.

CLAIM OF PRIORITY

I hereby claim the benefit under 35 U.S.C. § 120, of any United States application(s), or § 365(c) of any PCT international application designating the United States of America, listed below and, insofar as the above-identified specification, including claims, discloses and claims subject matter in addition to that disclosed in the prior copending application(s), listed below, I acknowledge the duty to disclose to the Office, all information which is known by me to be material to patentability as defined in 37 C.F.R. § 1.56, which became available between the filing date of the prior application and the national or PCT international filing date of this application.

PCT Application No. PCT/US99/22940, filed on October 13, 1999.

POWER OF ATTORNEY

I hereby appoint the practitioners associated with the Customer Number provided below (*i.e.*, the practitioners associated with the law firm of Price, Heneveld, Cooper, DeWitt and Litton) to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith. Please direct all correspondence to the address associated with that Customer Number.

Customer Number 000,277

All statements made herein of my own knowledge are true and all statements made on information and belief are believed to be true, and further, these statements are made with the knowledge that willful false statements and the like are punishable by fine or imprisonment, or both, under 18 U.S.C. § 1001, and that such willful false statements may jeopardize the validity of this application or any patent issued thereon.

1-00 Sole or First joint inventor:

06/22/01

Bruce J. Barrett Date

Citizenship: United States of America

Residence: 453 Baldwin

Birmingham, Michigan 48009 MI

Post Office Address: Same as above

2-00 Second joint inventor:

22/06/01

Oleg Gonopolsky Date

Citizenship: United States of America

Residence: 7128 North Merrybrook Street

West Bloomfield, Michigan 48322 MI

Post Office Address: Same as above

3-00 Third joint inventor:

6/22/01

Richard S. Scheuing Date
Citizenship: United States of America
Residence: 708 Dressler Lane
Rochester Hills, Michigan 48307 MI

09872850 . 062201